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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,706	04/10/2002	Guillermo De La Cueva Mendez	620-180	8608

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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
12/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/030,706	DE LA CUEVA MENDEZ ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,10,12-16 and 18* is/are pending in the application.

4a) Of the above claim(s) *18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 10, 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on 11/13/2007 under 37 DFR 1.116, in reply to the final rejection, has been considered and is hereby entered.

Upon further consideration, the finality of the previous office action is withdrawn.

Claims 1, 3, 10, 12-16, and 18 are pending. Claim 18 remains withdrawn. Claims 1, 3, 10, and 12-16 are currently under examination.

Claim Rejections Withdrawn

The rejection of claims 1-4, 10, and 12-16 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods in a target eukaryotic cell *in vitro*, does not reasonably provide enablement for the methods *in vivo*, is withdrawn in lieu of the rejection set forth below.

The rejection of claim 4 under 35 U.S.C. 112, second paragraph, because there is insufficient antecedent basis for the limitation "the human" in line 2, is withdrawn. The cancellation of said claim renders the rejection moot.

New Claim Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, and 10-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

The claims are drawn to methods of inhibiting cell proliferation of target eukaryotic cells (*in vitro*), comprising providing within eukaryotic cells ParD kid toxin and ParD kis antitoxin, under control so as to obtain selective cell cycle inhibition and/or killing of said target cells.

The specification and the art have shown that the kid/kis toxin/antitoxin system can be expressed in both bacterial and eukaryotic cells. So long as enough antitoxin is present to neutralize the toxin, cells are able to survive, but if the level of antitoxin decreases relative to the toxin, the toxin will inhibit cell proliferation or kill the cells.

However, those of skill in the art would be unable to perform the claimed method steps and achieve the stated goal of the method. The claimed method encompasses providing the toxin and antitoxin themselves as well as the nucleic acids which encode them. Said toxin and antitoxin must be "under control so as to obtain selective cell cycle inhibition and/or killing of said target cells." There is no means provided, either in the specification or the art to control the

activity of the toxin and antitoxin when administered in protein form, rather than as nucleic acids.

Further, to protect non-target cells, either the toxin must be down-regulated in non-target cells while not being altered in the target cells, or the antitoxin must be up-regulated in non-target cells while not being altered in the target cells. For this to happen, the inducers (or inhibitors) of these must be different in the target and non-target cells. For example, if IPTG were used to up-regulate antitoxin, it would do this in all of the cells present, without differentiating between target and non-target cells. To avoid this, the target and non-target cells must be provided with constructs that have different regulation schemes. The specification does not provide any specific means by which this could feasibly occur. One could individually inject cells with different constructs or treated target and non-target cells separately before combining them. However, in either of these cases, there is no asserted utility for such a method. Additionally, while there are targeting molecules available (such as cell-specific receptors), one would have to choose multiple targeting molecules so that one could reliably deliver the toxin/antitoxin with one regulation scheme to target cells (using the first targeting system) and use another targeting molecule to deliver the toxin/antitoxin with another regulation scheme to non-target cells. Presumably, the point of the invention is that the antitoxin is present to protect non-target cells from the action of the toxin. However, if one could reliably target the toxin to the target cells, there would be no need to provide antitoxin, since only the target cells would be affected by the toxin. Moreover, the claims are drawn to a method of inhibiting cell proliferation. The toxin is all that is required for this; the presence of the antitoxin is superfluous.

Therefore, in view of the lack of support in the art and specification, it would require undue experimentation on the part of the skilled artisan to make and use the invention as claimed; consequently the claims are not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 10, and 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the phrase, "the method comprising providing *within* eukaryotic cells ParD kid toxin and ParD kis antitoxin." The structure of the sentence implies that eukaryotic cells containing kid/kis are being provided. It is not clear what they are being provided to or how this would inhibit cell proliferation. It is suggested that applicant reword the claim so that it is clear that the toxin and antitoxin are being administered to the eukaryotic cells.

Claim 1 is rendered vague and indefinite because it is not clear how performing the method steps would result in the stated goal of the method. The goal of the method is to inhibit cell proliferation. Therefore, providing target cells with toxin would inhibit those cells. It is not clear why one would provide said cells with antitoxin. Furthermore, there is no method step which actually alters the levels of toxin and antitoxin such that cell proliferation would be inhibited. A step where the regulatory molecule is added is required. For example, if the antitoxin is to be down-regulated by the addition of some type of inhibitor, then that inhibitor must be added for said down-regulation, and consequently, inhibition of cell-proliferation, to occur.

Claims 14 and 15 are rendered vague and indefinite by their reference to non-target cells. It is not clear how these limitations would have any effect on the stated goal of the method. The invention is a method of inhibiting cell proliferation in target cells. Therefore, what happens in non-target cells is of no consequence.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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ROBERT A. ZEMAN
PRIMARY EXAMINER